Complete Summary

GUIDELINE TITLE

Screening and management of lipids.

BIBLIOGRAPHIC SOURCE(S)

University of Michigan Health System. Screening and management of lipids. Ann Arbor (MI): University of Michigan Health System; 2003 Apr. 15 p. [7 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Coronary heart disease
- Stroke

GUIDELINE CATEGORY

Management
Prevention
Screening
Treatment

CLINICAL SPECIALTY

Cardiology
Family Practice
Internal Medicine
Nursing
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Dietitians
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To present recommendations for primary and secondary prevention of coronary heart disease and stroke by outlining strategies for lipid screening, identifying patients who would benefit from treatment, and recommending appropriate treatment regimens

TARGET POPULATION

Adults 20-75 years of age without familial or severe dyslipidemias

INTERVENTIONS AND PRACTICES CONSIDERED

Screening

Primary Prevention

1. Initial laboratory tests: High-density lipoprotein cholesterol and total cholesterol (either fasting or nonfasting); assessment of coronary heart disease risk factors
2. Additional laboratory tests, such as a fasting lipid profile (total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides)
3. Assessment of secondary causes of hyperlipidemia

Secondary Prevention

Fasting lipid profile (total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides)

Treatment/Management

1. Lifestyle changes
    - Dietary interventions: Low-fat diet and reduction in saturated fats; inclusion of plant stanols (sitostanol and sitostanol esters, found in soft margarine); increase in soluble fiber (fruits and vegetables), omega-3 fatty acids (fish), linolenic acid (canola oil, soy, flax seed); and substitution of whole grains for processed flours
    - Smoking cessation
    - Weight loss
    - Regular physical exercise
    - Reduction in alcohol intake
2. Pharmacologic treatment

- Beta-hydroxy-beta-methylglutaryl-coenzyme A reductase inhibitors (statins): lovastatin (Mevacor®), pravastatin (Pravachol®), simvastatin (Zocor®), atorvastatin (Lipitor®), fluvastatin (Lescol®)
- Niacin: prescription (Niacor®, Niaspan®, Advicor® [niacin/lovastatin]) and over-the-counter
- Absorption inhibitors: bile acid resins (cholestyramine [Questran®], colesevelam [Welchol®], and colestipol [Colestid®]); ezetamibe (Zetia®)
- Fibrates (gemfibrozil [Lopid®], fenofibrate [Tricor®], benzafibrate, clofibrate)
- Monitoring of alanine aminotransferase (for statin patients) and alanine aminotransferase, glucose, and uric acid (for niacin patients)

3. Complementary and alternative treatments (considered but not recommended)
    - Estrogen replacement therapy and progestins for postmenopausal women
    - Ornish program: vegetarian diet, regular exercise, meditation, and yoga
    - Garlic
    - Red yeast rice
    - Fish oil

MAJOR OUTCOMES CONSIDERED

- Total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides levels
- Incidence of coronary heart disease and stroke, and rate of coronary events
- Total mortality associated with coronary heart disease
- Drug interactions and adverse effects

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The literature search for this update, began with results of the literature search performed in 1999 to develop the initial guideline. Those results were supplemented by relevant literature known to the authors that was published between 2000 and 2002, including reports of research studies and other publications. The literature search conducted in 1999 for this project was conducted prospectively using the major keywords of cholesterol, hyperlipidemia, lipoproteins hdl cholesterol, lipoproteins ldl cholesterol, triglycerides; consensus development conferences, practice guidelines, guidelines, outcomes and process assessment (health care); clinical trials, controlled clinical trials, multicenter studies, randomized controlled trials, cohort studies; adults; English language; and published in 1955-1999 on Medline (U.S. National Library of Medicine). Terms

used for specific topic searches within the major key words included mass screening, screening; drug therapy, statins, hydroxymethylglutaryl-CoA reductase inhibitors, antilipemic agents, niacin, bile acid sequesterant; and [diet, exercise, alternative/complementary medicine], each within [coronary arteriosclerosis, coronary disease, coronary thrombosis, peripheral vascular diseases, cerebrovascular disorders]. The search was conducted in components each keyed to a specific causal link in a formal problem structure (available from the guideline developer upon request). The search was supplemented with very recent clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was a single cycle.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational trials
D. Opinion of expert panel

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Conclusions were based on prospective randomized clinical trials if available, to the exclusion of other data; if randomized controlled trials were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Currently, generic lovastatin and atorvastatin are the most cost-effective agents for low density lipoprotein cholesterol lowering: lovastatin for ≤30%, atorvastatin for ≥30%.

Statins in primary prevention are cost-effective only in high-risk groups. In secondary prevention, they are cost-effective in all coronary heart disease (CHD) patients. Though not yet studied in elderly CHD patients (>74 years old), cost-effectiveness analyses have recently found statins cost-effective in this group as well.

Cost can be reduced by pill splitting. Every other day atorvastatin is effective at lipid lowering. However, evidence is accumulating suggesting that statin´s benefits may stem at least in part from non-lipid mechanisms such as their anti-inflammatory properties. Alternate-day therapy and doses lower than those used in clinical trials may therefore not achieve the outcomes benefits seen in trials.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

University of Michigan Health System guidelines are reviewed by leadership in departments to which the content is most relevant. This guideline concerning the screening and management of lipids was reviewed by members of the following departments: General Medicine; Medical Education; Pharmacy; Family Medicine; Hypertension; and Cardiology.

Guidelines are approved by the Primary Care Executive Committee and the Executive Committee of Clinical Affairs.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC): The following key points summarize the content of the guideline. Refer to the full text for additional information, including detailed information on dosing and cost of drugs and other interventions considered.

The levels of evidence [A-D] are defined at the end of the Major Recommendations.

- Primary Prevention

  Screening. Screen men aged 35-65 and women aged 45-65. Screening is optional for men aged 20-34 and women aged 20-44. Screening should be considered in both men and women aged 65-75 based on life expectancy.

Repeat screening in 5 years in patients with normal lipids [D*]. Screen with fasting or non-fasting total cholesterol (TC) and high-density lipoprotein (HDL) cholesterol [D*], or optionally, a full lipid or coronary heart disease (CHD) profile.

Treatment.

- Initial treatment: lifestyle modification—smoking cessation, diet, exercise, and weight reduction [A*].
- Drug therapy. Consider after 6 or more months if low-density lipoprotein cholesterol (LDL-C) remains elevated in those at intermediate to high risk for coronary heart disease [A*]. Determination of risk can be facilitated by using the Framingham-based Global Risk Score, which predicts 10 year risk of a coronary event [C*]

- Secondary Prevention

  Screening. Screen all patients with coronary heart disease or other atherosclerotic cardiovascular disease (ASCVD), including stroke and peripheral vascular disease [A*].

  Treatment.

  - All patients: Lifestyle modification [A*] and dietary consultation [D*].
  - Drug therapy: statin therapy should be considered for all patients.
    - Statins reduce mortality and CHD and atherosclerotic cardiovascular disease endpoints, probably even for patients whose baseline LDL-C is less than 100 mg/dl [A*].
    - Consider treating isolated low HDL-cholesterol, which has been shown to reduce CHD events, but not total mortality [A*].
    - Combination therapy may improve outcomes, but increases risk of myopathy [C*].
    - The optimal target for LDL-C has not been established. The guideline developers recommend following National Cholesterol Education Program (NCEP) guidelines: target <100 mg/dl.
- Cost Effectiveness

  Currently, generic lovastatin and atorvastatin are the most cost-effective agents for LDL-C lowering: lovastatin for ≤30%, atorvastatin for ≥30%.

- Special Populations

  Diabetes mellitus (DM) patients have a marked increased risk for CHD, and similar benefit from lipid lowering therapy. Patients with DM should be considered CHD equivalents, and screened and treated like CHD [A*].

Definitions:

Levels of Evidence

*Levels of evidence for the most significant recommendations.

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational trials
D. Opinion of expert panel

CLINICAL ALGORITHM(S)

Algorithms are provided in the original guideline document for:

- Primary Prevention of Coronary Heart Disease and Stroke
- Secondary Prevention of Coronary Heart Disease and Stroke

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence for each recommendation is given in brackets following the recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Benefits of Lowering Low-Density Lipoprotein Cholesterol Levels

- Low-density lipoprotein cholesterol (LDL-C) based drug therapy for primary prevention has been shown to reduce total mortality in high-risk populations.

  Lowering cholesterol has been shown to reduce the incidence of CHD, with each 10% reduction dropping the incidence by 20%.

  A recent large randomized clinical trial of statin therapy among patients with CHD, atherosclerotic vascular disease, or diabetes mellitus (DM) and a total cholesterol >135mg/dl showed a 25% relative risk reduction in all-cause mortality, stroke, myocardial infarction (MI), and need for revascularization. All subgroups benefited, including women and the elderly (age>70 years). Notably, patients at all levels of baseline LDL-C benefited to a similar degree, including the lowest LDL-C tertile of LDL-C <116mg/dl. Annual excess myopathy risk was about 0.01%. Treatment of 1000 patients with simvastatin would prevent 70-100 patients from having a major vascular event. Even those patients with a baseline LDL-C <100mg/dl (about 3500 patients) had a similar benefit. Statins are considered to have a class effect. There is no evidence that any one statin is better, though potency varies with the different agents.

Specific Benefits of Lifestyle Changes

- Diet: For primary prevention, 40-50% of patients with a high-risk level of low-density lipoprotein cholesterol (LDL-C) will reduce their LDL-C to borderline or low risk with 6 months of the National Cholesterol Education

Program (NCEP) Step II diet(<30% of calories from total fat, <7% of calories from saturated fat).

The degree of response to various dietary interventions, including an increase in soluble fiber, soy, omega-3 fatty acids, linolenic acid, and plant stanols and substitution of whole grains for processed flour correlates highly with the amount consumed and baseline low-density lipoprotein cholesterol levels. Prescribed diets should not be restrictive, but instead emphasize what should be eaten rather than what should not be eaten. There should be an increase in fruits and vegetables rich in fiber, an increase in fish (omega-3 fatty acids) and linolenic acid (canola oil, soy, flax seed) and a substitution of whole grain for processed flours and simple sugars. This diet is comparable to the Mediterranean diet, which has been shown to reduce coronary heart disease events beyond its impact on serum lipids.

- Smoking: In persons with coronary heart disease (CHD), smoking cessation reduces the coronary event rate by about 50% within one to two years of stopping. Among the benefits of smoking cessation is a 5-10% increase in high-density lipoprotein-cholesterol (HDL-C).
- Weight loss: Even modest weight loss counteracts the HDL-C lowering effect of the diet alone, lowers triglycerides, and causes further reduction in total cholesterol (TC) and LDL-C.
- Exercise: Regular physical exercise raises HDL-C and lowers triglycerides. Exercise alone has little effect on LDL-C. Exercise in combination with a low fat diet induces greater reduction in total cholesterol, LDL-C, and weight loss than dietary therapy alone. Even mild exercise (walking) done regularly (30 minutes, 4-5 times a week) has been shown to be beneficial. Weight training has also been shown to increase HDL-C.

Specific Benefits of Statins

Statins are the best studied of the lipid lowering drugs and show the most benefit, in terms of absolute LDL-C reduction and patient outcome.

Note: Specific drug therapies are summarized in Table 6 of the full-text original guideline document and drug interactions are summarized in Table 8 of the original guideline document.

Subgroups Most Likely to Benefit

- Women. Two large trials showed significant treatment benefit for women, and a recent meta-analysis on the effect of statins on risk of coronary heart disease (CHD) found similar benefit from statins in women. However, premenopausal women are at low risk of coronary heart disease.
- Diabetes mellitus (DM). Patients with DM type 2 have a 2 to 4 fold increased risk of CHD. Regarding treatment with a statin, diabetic subgroups in primary and secondary trials have similar benefit to non-DM patients.

POTENTIAL HARMS

- Adverse Effects. Adverse effects of statins include mild gastrointestinal disturbances, muscle aches, rash, and headache. Rhabdomyolysis occurs in <0.5% of patients but is increased in patients using niacin, fibrates,

cyclosporin, azoles, macrolides, and grapefruit juice. The risk is also increased in the cases of hepatic or renal dysfunction, hypothyroidism, serious infections, and advanced age.

Note: general cautions about drug class and drug interactions are provided in Table 6 and Table 8, respectively, in the original full-text guideline document.

- Exercise: Exercise must be tailored to the degree of coronary heart disease, with aerobic exercises at levels that do not precipitate angina.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Statins are contraindicated in pregnancy.
- Nicotine replacement therapy is contraindicated in unstable angina or acute myocardial infarction.
- Fibrates are contraindicated in severe renal or liver disease, pregnancy, or preexisting gall bladder disease.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

University of Michigan Health System. Screening and management of lipids. Ann Arbor (MI): University of Michigan Health System; 2003 Apr. 15 p. [7 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 May (revised 2003 Apr)

GUIDELINE DEVELOPER(S)

University of Michigan Health System - Academic Institution

SOURCE(S) OF FUNDING

University of Michigan Health System

GUIDELINE COMMITTEE

Lipid Therapy Guideline Team

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Team Leader: William Barrie, MD, General Medicine

Team Members: Van Harrison, PhD, Medical Education; Ujjaini Khanderia, PharmD, Pharmacy; Robert Kiningham, MD, Family Medicine; Melvyn Rubenfire, MD, Cardiology

Guidelines Oversight Team: Connie Standiford, MD; Lee Green, MD, MPH; Van Harrison, PhD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

Team Member; Company: Relationship

- William Barrie, MD; (None)
- Van Harrison, PhD; (None)
- Ujjaini Khanderia, PharmD; Novartis, Merck, Pfizer: Speakers Bureau; Phizer: Research Support
- Robert Kiningham, MD; (None)
- Melvyn Rubenfire, MD; Pfizer: Research Support

GUIDELINE STATUS

This is the current release of the guideline.

The guideline updates a previous version: Screening and management of lipids. Ann Arbor (MI): University of Michigan; 2000 May. 13 p.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the University of Michigan Health System Web site.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

The following is available:

- Cholesterol patient education handout. University of Michigan Health System; 2003. Various p.

Electronic copies: Available from the University of Michigan Health System Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This summary was completed by ECRI on January 26, 2001. The information was verified by the guideline developer on March 12, 2001. This summary was updated on September 6, 2001 following the withdrawal of the drug Baycol (Cerivastatin). This summary was updated again on January 19, 2004. The information was verified by the guideline developer on February 6, 2004.

Date Modified: 11/15/2004